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10/502,510	05/02/2005	Mohamed Raafat El-Gewely	04-585	3954

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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,510	EL-GEWELY, MOHAMED RAAFAT	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 27-53* is/are pending in the application.

4a) Of the above claim(s) *1,27-37,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/6/05; 2/25/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 2-26 have been cancelled.

Claims 1 and 27-53 are currently pending.

Claims 1, 27-37, 52 and 53 have been withdrawn.

Claims 38-51 are being examined in this application.

Election/Restrictions

2. Applicant's election without traverse of Group 3 (claims 38-51) in the reply filed on 5/19/2008 is acknowledged.

3. Claims 1, 27-37, 52 and 53 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/19/08.

Priority

4. This application is filed under 35 U.S.C 371 of PCT/GB03/00291 (filed on 1/23/2003).

5. Receipt is acknowledged of papers (UK 0201522.0 and UK 0201523.8) submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The IDS filed on 5/6/05 and 2/25/08 have been considered. See the attached PTO 1449 forms. Please note the typographic error corrections in IDS filed on 2/25/08.

Specification

7. The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. (e.g. See p.5) Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Sequence Rule Compliance

8. "In order to expedite the processing of applications, minor errors pertaining to compliance with the sequence rules may be handled with the first Office action." See MPEP 2427.01.

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) below:

The instant disclosure recites lists of sequences in the specification (e.g. see p. 13, 17, 28-29, etc.), which sequences are not identified by their corresponding SEQ ID Nos. The instant

disclosure also recites lists of sequences in the drawings (e.g. Figure 3), which sequences are not identified by their corresponding SEQ ID Nos in the "BRIEF DESCRIPTION OF THE FIGURES AND TABLES" of the instant specification. Applicants are requested to amend the instant specification and/or claims accordingly.

In order to be fully responsive to the instant Office action, applicant must fully comply with the Sequence Rule as discussed supra.

10. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. MPEP 608.01

Claim Rejections - 35 USC § 112

Second paragraph of 35 U.S.C. 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 38-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A.) Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the "screening" steps. The instant claim 38 seems to only

recite one method step of "introducing the library into host cells…" The instant claim 38 does not appear to recite the essential method steps of detecting the "reporter".

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Shibata

14. Claims 38-41, 45-47 and 51 are rejected under **35 U.S.C. 102(b)** as being anticipated by Shibata et al (EP 0989136; 3/29/2000; cited in IDS).

The instant claims recite "a method of screening a library of molecules for the ability of members of the library to restore or modify the function of a target protein in an intra-cellular environment, the method comprising introducing the library into host cells having a reporter system that allows for the identification of those cells in which the function of the target protein has been restored or modified."

Shibata et al, throughout the publication, teach various methods of screening a library of peptides with a reporter gene assay system (e.g. Abstract; pp.19+). The reference teaches cells comprising a reporter system (e.g. pp.19-20, bridging), which read on the host cells having a

reporter system of **clm 38**. The reference also teaches introducing "test compounds" (i.e. a library of molecules) into the host cells (e.g. p.20, lines 40+; Tables 3-4), which reads on the step of introducing the library into host cells as recited in **clm 38**. The reference also teaches measuring the activation of p53 (i.e. restoration/modification of p53 activity) through the reporter gene expression (e.g. pp.19+; [0095]), which reads on the target protein function of **clm 38**.

The p53 protein of the reference also reads on the nucleic acid binding protein as the reference teaches the protein binds to "P53 responsive element" (e.g. pp.19-20, bridging), which reads on the target protein of **clms 39** and **40**.

The reference teaches the reporter system comprise a reporter gene (e.g. luciferase) and a "P53 responsive element" in the transcription regulatory region (e.g. pp.19-20), which the reporter gene construct reads on the reporter system of **clm 41**.

The reference teaches transfecting the reporter plasmid into the host cells (e.g. [0104]+), which reads on the transfection step of **clm 45**.

The reference teaches the test compounds are a collection of peptides (e.g. pp.6+), which reads on the peptide library of **clm 46**.

The reference teaches the peptides are of various amino acids (e.g. Table 1), which the peptides read on the peptides of **clm 47**. The transitional phrase "have" is interpreted as open-ended and thus the peptides of the instant claims can "have" additional amino acid residues. See MPEP 2111.03.

The reference teaches using human cells (e.g. p.20, lines 46+), which reads on the eukaryotic cells of **clm 51**.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Shibata and Thornborrow

16. Claims **38-42**, **45-47** and **51** are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al (EP 0989136; 3/29/2000; cited in IDS), in view of Thornborrow et al (JBC. Vol.274(47): 33747-33756; 1999; cited in IDS).

Shibata et al, throughout the publication, teach various methods of screening a library of peptides with a reporter gene assay system as discussed supra. The above rejection over Shibata et al under 35 USC 102(b) is herein incorporated by reference in its entirety.

Shibata et al do not explicitly teach the reporter gene construct is linked t a p21 or BAX promoter as recited in **clm 42**.

However, Thornborrow et al teach using reporter gene constructs with either p21 or BAX promoter region that contains p53 response elements (or p53 binding regions) (e.g. p.33748, left col., para 3), which the promoters read on the promoters recited in **clm 42**. The reference also teaches the p21 and BAX promoters are regulated by p53, and the regulation is important in various cellular mechanisms (e.g. p.33747). Thus, there is a great need to understand the interaction between the promoters and p53.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to using p21 or BAX promoter region in the reporter gene construct for testing p53.

A person of ordinary skill in the art would have been motivated at the time of the invention to use p21 or BAX promoter region in the reporter gene construct for assaying p53, because p21 and BAX are known to substrate for p53 as taught by both Shibata et al and Thornborrow et al. In addition, due to the need to understand the interaction between p53 and its regulatory elements for various important cellular functions, a person of ordinary skill in the art would have been motivated at the time of the invention to use p21 or BAX promoters. In addition, because the both references teaches using reporter gene construct with p53 responsive elements (such as various promoter regions) for testing p53, it would have been obvious to one skilled in the art to substitute one known p53 responsive element (SV40 early promoter region) for the other (p21 or BAX promoter region) to achieve the predictable result of detecting measuring/testing p53 activation/function in a reporter gene assay system.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since both of the cited references have demonstrated the success of using reporter gene assays with various elements.

Shibata and Others

17. Claims **38-47** and **51** are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al (EP 0989136; 3/29/2000; cited in IDS) and Thornborrow et al (JBC. Vol.274(47):

33747-33756; 1999; cited in IDS), as applied to claims 38-42, 45-47 and 51 above, and further in view of Skarnes (US 5,767,336; 6/16/1998).

Shibata et al, throughout the publication, teach various methods of screening a library of peptides with a reporter gene assay system as discussed supra.

Thornborrow et al teach using reporter gene constructs with either p21 or BAX promoter region that contains p53 response elements as discussed supra.

The above rejection over Shibata and Thornborrow references under 35 USC 103(a) is herein incorporated by reference in its entirety.

The combination of the Shibata and Thornborrow references does not explicitly teach the reporter gene product include a secretion signal peptide as recited in **clm 43**, and a transmembrane domain as recited in **clm 44**.

However, Skarnes et al teach generating reporter gene construct having secretion signals and transmembrane domains (e.g. cols.3, lines 20+), which read on the signal peptide and transmembrane domain as recited in **clms 43** and **44**. The reference also teaches the need to generate reporter gene encoding for fusion proteins having secretion signal and transmembrane domains for studying secretary proteins (e.g. cols.1-2).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to generate reporter proteins with secretion signal and transmembrane domains.

A person of ordinary skill in the art would have been motivated at the time of the invention to generate fusion reporter proteins having secretion signals and transmembrane domain, because including secretion signals and transmembrane in fusion reporter proteins are

known and routine in the art as taught by Skarnes. As the Skarnes reference teaches the advantages of including secretion signals and transmembrane domains so that secretary proteins can be conveniently studied (e.g. cols.1-2), a person ordinary skill in the art would have been motivated at the time of the invention to generate fusion reporter proteins having secretion signals and transmembrane domain. In addition, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating fusion reporter proteins having secretion signals and transmembrane domains, as taught by Skarnes, to improve the reporter protein assay for the predicable result of enabling standard reporter gene assay system.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since all of the cited references have demonstrated the success of using reporter gene assays with various elements.

Shibata and Others

18. Claims **38-51** are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al (EP 0989136; 3/29/2000; cited in IDS), Thornborrow et al (JBC. Vol.274(47): 33747-33756; 1999; cited in IDS), and Skarnes (US 5,767,336; 6/16/1998) as applied to claims 38-47 and 51 above, and further in view of Noaln et al (WO 97/27212; 7/31/1997; cited in IDS).

Shibata et al, throughout the publication, teach various methods of screening a library of peptides with a reporter gene assay system as discussed supra.

Thornborrow et al teach using reporter gene constructs with either p21 or BAX promoter region that contains p53 response elements as discussed supra.

Skarnes et al teach generating reporter gene construct having secretion signals and transmembrane domains, as discussed supra.

The above rejection over Shibata, Thornborrow and Skarnes references under 35 USC 103(a) is herein incorporated by reference in its entirety.

The combination of the Shibata, Thornborrow and Skarnes references does not explicitly teach the library is introduced into the host cells as nucleic acid constructs as recited in **clm 48** as well as the size of the library recited in **clm 50**. The reference also does not explicitly teach the peptide library has the sequence of M-G/M/V-(X)n as recited in **clm 49**.

However, Noaln et al teach making and using peptide libraries in target screening assays (e.g. Abstract). The reference teaches generating nucleic acid constructs encoding for the peptides and introducing the constructs into cells (e.g. p.23), which reads on DNA constructs of **clm 48**. The reference also teaches the size of the peptide library are various such as 10^7 peptides (e.g. p.20, lines 4+), which reads on the library size of **clm 50**. The reference also teaches using peptide library with conserved consensus amino acid residues such as the ones with M and G residues (e.g. p.7; p.8; p.22), which reads on the sequence of **clm 49**.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to screen a library with various sizes and to screen a peptide library with various sequences using encoding nucleic acid constructs.

A person of ordinary skill in the art would have been motivated at the time of the invention to use encoding nucleic acid constructs to introduce peptides into cells, because using nucleic acid constructs are known and routine in the art as taught by Noaln et al. In addition, it would have been obvious to one of ordinary skill in the art to apply the standard technique of

using encoding nucleic acid constructs to produce peptides in cells as taught by Noaln et al, to improve the peptide library production inside cells for the predicable result of enabling standard peptide library screening assays inside cells.

A person of ordinary skill in the art would have been motivated at the time of the invention to use peptide library of various sizes, because peptide library of various sizes are known and routine in the art as taught by Noaln et al. In addition, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating peptide library of large size (such as at least 500 different members) as taught by Noaln et al, to improve the peptide library diversity and screening efficiency for the predicable result of enabling standard peptide library screening assays.

A person of ordinary skill in the art would have been motivated at the time of the invention to screen peptide library generated with certain conserved consensus amino acid residues depending on the screening target, because using peptides with conserved amino acid residues for targeted screening are known and routine in the art as taught by Noaln et al. In addition, because both of the Shibata and the Noaln references teaches screening peptide libraries, it would have been obvious to one skilled in the art to substitute one type of peptide libraries (with one type of consensus sequence) for the other (e.g. sequences with M and G residues) to achieve the predictable result of screening peptide libraries in a reporter gene assay system.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since all of the cited references have demonstrated the success of using reporter gene assays with various elements.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 38-51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 28-49 of copending Application No. 10/493,582 (PGPUB 20070128657; hereinafter referred to as the '582 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '582 application read on the instant claimed method.

The '582 application claims a method of screening a library of peptides using reporter system as recited in claim 1, which reads on the method of the instant claim 38.

The '582 application also claims various components of the reporter system, the target protein, the size of the library, etc., (as recited in claims 28-39), which reads on the instant claimed reporter system, target protein, etc., as recited in the instant claims 39-51.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SUE LIU/
Examiner, Art Unit 1639
8/26/08